## REMARKS

After entry of the foregoing amendments, Claims 22-29 have been amended. By the foregoing amendments, Claims 30-31 are cancelled without prejudice. Therefore, Claims 22-29 and 32-34 remain present for examination. The amended claims are supported by the specification and the claims as originally filed. Therefore, no new matter has been added. The specific changes to the amended claims are shown above with the insertions being underlined and the ~~deletions shown stricken through.~~

Applicants respond below to the formal matters and to the specific rejections and objections raised by the Examiner in the Office Action of March 12, 2003.

Discussion of Formal Matters

*Priority:*

The Office Action granted priority to the filing date of PCT/US00/05601, filed on March 1, 2000. Applicants acknowledge the date of March 1, 2000 for examination of the instant claims. Applicants make no admission as to the propriety of that date for priority and reserve the right to later address the same.

*Title Objection:*

According to the Office Action, the title of the invention was not descriptive. The title has been amended as set forth above to be more descriptive of the invention set forth in the elected claims. Therefore, Applicants request withdrawal of the objection to the title.

*Claim Objections:*

Claims 22-31 were objected to for identifying a sequence by reference to a figure with the SEQ ID NO in parenthesis. As set forth above, Claims 30-31 have been cancelled and Claims 22-29 have been amended to recite "the polypeptide having the sequence of SEQ ID NO:2." Thus, Applicants respectfully request withdrawal of the objections to pending Claims 22-29.

Discussion of Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 22-34 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards

as the invention. In particular, the Office Action alleges that Claims 22-27, 30 and 31 are not clear because they recite "the extracellular domain."

As set forth above, Claims 30-31 have been cancelled and Claims 22-27, 30 have been amended to remove reference to "the extracellular domain." In view of the amendments to Claims 22-27, 30 and 31, the claims are clear and definite. Therefore, withdrawal of the § 112, second paragraph, rejections is respectfully requested.

Discussion of Rejections under 35 U.S.C. § 112, First Paragraph

*Enablement*

Claims 22-27, 30-31, and 33-34 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. According to the Office Action, the specification, while being enabling for claims limited in scope to a polypeptide of SEQ ID NO:2, and a polypeptide of SEQ ID NO:2 lacking its associated signal peptide, does not reasonably provide enablement for claims to various percentage variants and fragments.

"To be enabling, the specification of a patent must teach those skilled in the art to make and use the full scope of the claimed invention without 'undue experimentation' ... Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." *See In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993). Enablement "is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive." *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986).

Amended Claims 22-27, as well as Claims 33-34 are enabled. As stated in the Office Action, claims to a polypeptide having the sequence of SEQ ID NO:2, and a polypeptide having the sequence of SEQ ID NO:2 lacking its associated signal peptide, are enabled. Thus, amended Claim 27 is enabled.

Claims 22-26 and 33-34, which incorporate all of the limitations of Claim 22, are also enabled. As set forth above, Claims 22-29 have been amended to remove reference to "the extracellular domain." Claims 22-26 have been amended to include a functional limitation associated with the percentage variants, specifically that the isolated polypeptide has the ability to induce chondrocyte redifferentiation.

The claims as amended are enabled because, given the teaching of the specification, one of ordinary skill in the art can easily make and use the isolated polypeptides, which have the ability to induce chondrocyte redifferentiation, without undue experimentation. For example, the specification at pages 109-113 provides detailed teaching on how to make polypeptide variants. Those teachings include, for example, how to make variations in the full-length native sequences, how to make fragments, how to make substitutions and how to make modifications.

Furthermore, Example 36 at page 166 of the specification provides working examples and an assay protocol for determining if a polypeptide induces redifferentiation of chondrocytes.

Thus, the specification provides ample guidance and direction for making and using the claimed polypeptides with little or no experimentation. One of ordinary skill in the art can easily follow the teachings of the specification to make polypeptide percentage variants as specified in the claims. The skilled artisan also can easily determine using the assay of Example 36 that the polypeptide variant has the claimed functionality. Therefore, enablement is commensurate in scope with the amended claims. For these reasons, reconsideration and withdrawal of the enablement rejection in view of the amendments to the claims is respectfully requested.

*Written Description*

Claims 22-27, 30, and 33-34 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors possessed the claimed invention at the time of filing the application. According to the Office Action, the claims are drawn to a genus of polypeptides that is defined only by sequence identity; the claims do not require, *inter alia*, that the polypeptide possess any particular biological acitvity.

To satisfy the written description requirement, a patent application must describe the invention in sufficient detail that one of skill in the relevant art could conclude that the inventor was in possession of the claimed invention at the time the application was filed. *See Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, (Fed. Cir. 1991). All disclosed distinguishing identifying characteristics are to be considered, including the level of skill and knowledge in the art, partial structures, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, method of making, and any combinations thereof. *See* M.P.E.P. § 2163.

Claim 27 is fully described because the specification provides the sequence for the isolated polypeptide as recited in the claims. Certainly, the specification describes both an isolated polypeptide comprising the amino acid sequence of the polypeptide having the sequence of SEQ ID NO:2 and an isolated polypeptide comprising the amino acid sequence of the polypeptide having the sequence of SEQ ID NO:2 lacking its associated signal peptide. Similarly, the specification certainly describes an isolated polypeptide comprising the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203581. Therefore, Claim 27 is fully described.

Also, amended Claims 22-26, and Claims 33-34 depending from Claim 22, are described in sufficient detail to show possession of the claimed invention by the inventors at the time of filing the application. As discussed above, independent Claims 22-26 have been amended to include the functional limitation for biological activity that "said isolated polypeptide has the ability to induce chondrocyte redifferentiation." In view the amendment, the independent claims and the claims depending therefrom or incorporating their limitations, are fully described because the genus of isolated polypeptides is described by sufficient identifying characteristics to show possession. Reconsideration and withdrawal of the written description rejection is therefore respectfully requested.

Discussion of Rejections under 35 U.S.C. § 102

Claims 22-27, 30 and 31 were rejected under 35 U.S.C. § 102(b) as being anticipated by Dumas et al., WO 99/06551-A2 (referred to hereafter as "Dumas"). Also, Claims 22-24, 30 and 31 were rejected under § 102(b) as being anticipated by Strachan et al., WO 99/55865-A1. Finally, Claims 22-24, 30 and 31 were rejected under 35 U.S.C. § 102(e) as being anticipated by Strachan, U.S. Patent No. 6,150,502.

Dumas, Strachan et al. and Strachan do not anticipate amended Claims 22-29 or Claims 32-34. To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). "Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. ... There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of

ordinary skill in the field of the invention." *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991).

*Dumas § 102(b) Rejection*

According to the Office Action, Dumas discloses a secreted polypeptide that has 128 amino acids, of which 124 amino acids are identical with amino acids 1-124 of SEQ ID NO:2. Therefore, the Office Action asserts that Dumas anticipates the claims "as being a polypeptide having sequence identity to the amino acid sequence of the extracellular domain of the polypeptide of SEQ ID NO:2."

The polypeptide disclosed by Dumas having 128 amino acids is different from the polypeptide having the sequence of SEQ ID NO:2, which has 246 amino acids. Dumas discloses a peptide that is identical only to 50.4% of the polypeptide having the sequence of SEQ ID NO:2. Therefore, Dumas disclosed a different polypeptide. Also, identity of 50.4% is far less than the 80% sequence identity recited in Claim 22, for example. Therefore, Dumas does not anticipate Claims 22-27 because Dumas did not disclose the same polypeptide, that is one having the recited identity to the sequence of SEQ ID NO:2 or one having the sequence of SEQ ID NO:2.

Furthermore, Claims 22-26 as amended require that the polypeptide have the ability to induce chondrocyte redifferentiation. Dumas does not teach a polypeptide having the ability to induce chondrocyte redifferentiation. Therefore Dumas does not anticipate because it does not teach each and every limitation of the claims.

*Strachan § 102(b) Rejection*

According to the Office Action, Strachan et al. discloses a polypeptide that has 105 amino acids, of which 101 amino acids are identical with amino acids 1-105 of SEQ ID NO:2. Therefore, the Office Action asserts that Strachan et al. anticipates the claims "as being a polypeptide having 90% sequence identity to the amino acid sequence of the extracellular domain of the polypeptide of SEQ ID NO:2."

The polypeptide disclosed by Strachan et al. having 105 amino acids is different from the polypeptide having the sequence of SEQ ID NO:2, which has 246 amino acids. The peptide disclosed by Strachan et al. is identical to only 39.8% of the polypeptide having the sequence of SEQ ID NO:2. Thus, Strachan et al. disclosed a different polypeptide. Further, the identity of

only 39.8% is far less than the 80% sequence identity recited in Claim 22, for example. Therefore, Strachan et al. does not anticipate Claims 22-24 because Strachan et al. did not disclose the same polypeptide, that is one having the recited identity to the sequence of SEQ ID NO:2 or one having the sequence of SEQ ID NO:2.

Additionally, Claims 22-24 as amended require that the polypeptide have the ability to induce chondrocyte redifferentiation. Strachan et al. does not teach a polypeptide having the ability to induce chondrocyte redifferentiation. Therefore Strachan et al. does not anticipate because it does not teach each and every limitation of the claims.

The Office Action stated that Strachan, U.S. Patent No. 6,150,502, disclosing SEQ ID NO:147 with 105 amino acids, anticipates Claims 22-24, 30 and 31 under § 102(e) for the same reason as stated above with regard to Strachan et al. Thus, for the same reasons set forth above, Strachan also does not anticipate the claims.

Applicants, therefore, request that the Examiner reconsider and withdraw the rejections based on 35 U.S.C. § 102.

Discussion of Rejections under 35 U.S.C. § 103

Claims 33 and 34 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Dumas, Strachan et al., or Strachan in view of Capon et al., U.S. Patent No. 5,116,964.

To establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

The primary references alone or in combination with Capon et al., still do not teach or suggest all of the limitations of Claims 33 and 34, which depend from or incorporate all of the limitations of amended Claim 22. As discussed above, the polypeptides disclosed by Dumas, Strachan et al., and Strachan are different from the isolated polypeptide having at least 80% sequence identity to the sequences recited in Claim 22, including the polypeptide having the sequence of SEQ ID NO:2. Capon et al. was cited as a reference that allegedly discloses a novel polypeptide fusion comprising an immunoglobulin Fc region and a target protein sequence. However, the primary references, even if combined with Capon et al, still do not teach or suggest

all of the limitations of Claims 33 or 34 because the cited references do not disclose a chimeric polypeptide comprising the isolated polypeptide of Claim 22. In addition, the primary references do not teach polypeptides having the ability to induce chondrocyte redifferentiation as set forth in the claims.

Therefore, Claims 33-34 are not obvious in view of the combination of Dumas, Strachan et al. or Strachan with Capon et al., and withdrawal of the rejections under § 103(a) is specifically requested.

## CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. Any claim amendments which are not specifically discussed in the above remarks are made in order to improve the cosmetics of the claims. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: June 12, 2003

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